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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,517	09/16/2003	Sang Yup Lee	Q77445	2292

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
11/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/662,517	LEE ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6-9,11,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-9,11 and 15* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/26/07 has been entered.

Claims 3, 5, 10 and 12-14 have been canceled. Claims 1, 2, 4, 6-9, 11, 15, and 16 are still at issue and are present for examination.

Applicants' arguments filed on 3/26/07, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a),

the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 6-9, 11 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramirez et al. and Lamouse-Smith et al. in view of Martens et al., Swiss-Prot Accession No. P29460, Hatamoto et al. (JP 09/009982) and Koonin et al.

Ramirez et al. and Lamouse-Smith et al. teach that recombinant protein production in *E. coli* can be improved by increasing the available levels of amino acids present in the recombinant protein in levels substantially above the levels of that amino acid in *E. coli* proteins. Lamouse-Smith et al. specifically teach that serine-family amino acids in particular are often present in higher levels in recombinant proteins and that the metabolic burden imposed by amino acid composition can be alleviated by supplementing the cell with required precursors.

Martens et al. teach the usefulness of IL-12 p40 as an IL-12 antagonist for the treatment of septic shock and other conditions and the recombinant production of high levels of this protein in *E. coli*.

Swiss-Prot Accession No. P29460 teaches the amino acid sequence of human IL-12 p40 showing that this protein has 3.3% cysteine residues.

Koonin et al. teach the average amino acid composition of *E. coli* proteins (see Table 1) and specifically that on average *E. coli* proteins have only 1.1% cysteine residues.

Hamamoto et al. teach methods of increasing the amount of cysteine produced in *E.coli* comprising transforming *E. coli* with a plasmid encoding the *E.coli* genes for *cysE*, *cysK* and *pta* and teach a vector encoding these genes.

As Martens et al. teach that a skilled artisan would clearly desire to produce high levels of IL-12 p40 in *E. coli* and a comparison of Swiss-Prot Accession No. P29460 with the amino acid composition of *E. coli* proteins of Koonin et al. shows that this protein has 3 times more cysteine than the average *E. coli* protein, it would have been obvious to produce the IL-12 p40 in an *E. coli* cell have increased levels of cysteine, such as the transformed cells of Hamamoto et al. One of skill in the art would have been motivated to use the cells of Hamamoto et al. by the disclosures of Ramirez et al. and Lamouse-Smith et al. that recombinant protein production in *E. coli* can be improved by increasing the available levels of amino acids present in the recombinant protein in levels substantially

above the levels of that amino acid in *E. coli* proteins. Furthermore, one of skill in the art would have found it obvious to either include the gene encoding IL-12 p40 on the same vector as the *cysE*, *cysK* and *pta* genes of Hamamoto et al. or alternatively to include it on a separate vector.

Applicants arguments in response to this rejection are unclear and confusing and thus not persuasive. Applicants state that "Lamouse teaches that when an amino acid is present in a recombinant protein at levels significantly higher than that present in host cellular proteins, the amino acid becomes a limiting factor in expression level. In other words, an increase in specific amino acid level does not directly induce an increase in specific protein production; rather, the production of specific amino acid is inhibited by feedback inhibition regulatory network." However the second sentence is not a recapitulation of the first in different words as suggested by applicants but instead a complete change of the meaning of the first statement. As such it is not clear what applicants are arguing. Applicants argue that "If cysteine increases in host cellular protein, cellular regulating systems will inhibit cysteine production and IL-12 p40 serine-rich protein production will not increase". However, this is not persuasive as it misstates what would occur. A correct statement of what would

be expected is "If the level of free cysteine increases intracellularly in the recombinant host, cellular regulating systems will inhibit cysteine production". However, in view of the disclosures of Lamouse-Smith et al. and Ramirez et al., a skilled artisan would not expect the levels of free cysteine to be high at all, as all available cysteine would be expected to be incorporated into recombinant protein. In other words the levels of free cysteine intracellularly in the recombinant host would be low. The remaining pages of applicants arguments discuss a variety of features of the present invention but their relevance to the instant rejection is not clear as the instant rejection suggested the construction of the claimed recombinant hosts and methods of using them for a different reason than that discussed by applicants. None of applicants discussion appears to address what the rejection suggests but only whether applicants reasons were obvious. As such the rejection is maintained.

Claim 16 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not suggest the specific vectors recited in claim 16.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner

can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652